

**Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of Claims:**

1. (Original) A method for synthesising one or more bifunctional complexes each comprising a) a molecule resulting from the reaction of a plurality of chemical entities and b) an identifier polynucleotide identifying one or more or all of the chemical entities having participated in the synthesis of the molecule, said method comprising the steps of

- i) providing a plurality of building blocks at least some of which comprise one or more chemical entities linked to an identifier oligonucleotide,
- ii) providing one or more connector oligonucleotides capable of hybridising to the identifier oligonucleotides of the building blocks provided in step i),
- iii) hybridising identifier oligonucleotides of the building blocks to the one or more connector oligonucleotides,
- iv) ligating identifier oligonucleotides hybridised to connector oligonucleotide(s), thereby generating an identifier polynucleotide comprising covalently linked identifier oligonucleotides at least some of which are linked to one or more chemical entities,

- v) separating the identifier polynucleotide from the one or more optionally ligated connector oligonucleotide(s),
- vi) reacting the chemical entities linked to the identifier polynucleotide in the absence of hybridisation between identifier oligonucleotides and connector oligonucleotides, and
- vii) obtaining a bifunctional complex comprising a molecule resulting from the reaction of the chemical entities, said molecule being linked to an identifier polynucleotide identifying at least some and preferably all of the chemical entities having participated in the synthesis of the molecule.

2. (Original) The method of claim 1, wherein at least one building block identifier oligonucleotide or at least one connector oligonucleotide is attached to a solid support.

3. (Currently amended) The method of claim 1 comprising the steps of

immobilising at least one building block comprising an identifier oligonucleotide to a solid support,

hybridising said immobilized building block oligonucleotide to a first connector oligonucleotide,

hybridising at least one additional building block oligonucleotide to said first connector oligonucleotide,

ligating building block oligonucleotides hybridised to the connector oligonucleotide,

separating the connector oligonucleotide from the ligated building block oligonucleotides,

reacting one or more chemical entities associated with different building block oligonucleotides, which are ligated and separated ~~building block oligonucleotides~~,

obtaining a first bifunctional complex comprising a first molecule, ~~or first molecule precursor~~, linked to a first identifier polynucleotide identifying at least some of the chemical entities having participated in the synthesis of the first molecule, ~~or molecule precursor~~,

wherein said first bifunctional complex is optionally immobilised to the solid support.

4. (Original) The method of claim 3, wherein said chemical entities are reacted in a reaction compartment from which the connector oligonucleotide has been removed in a washing and/or separation step prior to the reaction of said chemical entities.

5. (Currently Amended) The method of claim 3 comprising the steps of

providing a second connector oligonucleotide,

hybridising said second connector oligonucleotide to the identifier polynucleotide of said first bifunctional complex comprising a first molecule ~~precursor~~,

hybridising at least one further oligonucleotide of a building block to said second connector oligonucleotide,

ligating building block oligonucleotides hybridised to the second connector oligonucleotide, wherein at least one of said building block oligonucleotides are hybridised to the first identifier polynucleotide,

separating the second connector oligonucleotide from the ligated building block oligonucleotides, ~~for example by diverting the second connector oligonucleotide to another compartment,~~

reacting the first molecule ~~precursor~~ with the one or more chemical entities associated with the ligated building block oligonucleotide(s),

obtaining a second bifunctional complex comprising a second molecule, ~~or second molecule precursor,~~ linked to a second identifier polynucleotide identifying at least some of the chemical entities having participated in the synthesis of the second molecule, ~~or second molecule precursor,~~

wherein said second bifunctional complex is optionally immobilised to a solid support.

6. (Previously Presented) The method of claim 1, wherein each step for providing a connector and a building block is repeated for different connector oligonucleotides and different further building blocks.

7. (Currently Amended) The method of claim  $\pm$  2, wherein said bifunctional complex, or a plurality of such complexes, is released from the solid support to which it is immobilised.

8. (Previously Presented) The method of claim 1, wherein different bifunctional complexes are generated in different reaction compartments,

wherein at least some of said different bifunctional complexes are combined in a further reaction compartment comprising a plurality of further connector oligonucleotides,

wherein at least two of said different bifunctional complexes hybridise to a further connector oligonucleotide,

wherein the molecule precursor part of said complexes react, thereby generating a further molecule in the form of a reaction product,

wherein the identifier polynucleotides of said bifunctional complexes are optionally covalently linked prior to, during, and/or after, the reaction of the molecule precursors,

wherein the covalently linked identifier polynucleotides are optionally separated from the further connector oligonucleotide prior to or after reaction of said molecule precursors.

9. (Currently Amended) A method for synthesising a bifunctional complex comprising a molecule resulting from the reaction of a plurality of chemical entities, wherein said molecule is linked to an identifier polynucleotide identifying one or more of the chemical entities having participated in the synthesis of the molecule, said method comprising the steps of

- i) providing a plurality of building blocks selected from the group consisting of

- a) building blocks comprising an identifier oligonucleotide linked to one or more chemical entities,
  - b) building blocks comprising an identifier oligonucleotide linked to one or more reactive groups, and
  - c) building blocks comprising an identifier oligonucleotide comprising a spacer or hybridisation region, wherein said building blocks comprising a spacer or hybridisation region are preferably connector oligonucleotides to which building blocks of groups a) and b) can hybridise,
- ii) generating a hybridisation complex comprising at least n building blocks by hybridising the identifier oligonucleotide of one building block to the identifier oligonucleotide of at least one other building block,

wherein n is an integer of 4 or more

wherein at least 3 of said at least n building blocks comprise a chemical entity,

wherein no single identifier oligonucleotide is hybridised to all of the remaining identifier oligonucleotides,

wherein optionally at least one of said building blocks of group c) is immobilised to a solid support, thereby providing a handle to which an

oligonucleotide of at least one building block of groups a) or b) can hybridise,

- iii) covalently linking identifier oligonucleotides of building blocks comprising one or more chemical entities, thereby obtaining at least one identifier polynucleotide comprising covalently linked identifier oligonucleotides each associated with one or more chemical entities,
- iv) optionally separating said identifier polynucleotide obtained in step iii) from any optionally immobilised connector oligonucleotides hybridised thereto, wherein said separation optionally comprises the step of diverting said identifier polynucleotide comprising covalently linked identifier oligonucleotides each associated with one or more chemical entities to a different reaction compartment, thereby separating said identifier polynucleotide from said optionally immobilised connector oligonucleotides
- v) reacting said at least 3 chemical entities linked to the identifier polynucleotide in the absence of hybridisation between identifier oligonucleotides and connector oligonucleotides, and
- vi) obtaining a bifunctional complex comprising a molecule resulting from the reaction of a plurality of chemical entities, wherein said molecule is linked to an identifier polynucleotide identifying

one or more of the chemical entities having  
participated in the synthesis of the molecule;

preferably, all chemical entities to be reacted are linked to  
the same identifier polynucleotide.

10. (Original) The method of claim 9 wherein a plurality  
of different bifunctional complexes is obtained by repeating  
the method steps for different building blocks.

11. (Cancelled)

12. (Currently Amended) The method of claim 1,  
wherein a plurality of molecules are synthesized,  
wherein the plurality of synthesised molecules are  
selected from the group consisting of  $\alpha$ -peptides,  $\beta$ -peptides,  
 $\gamma$ -peptides,  $\omega$ -peptides, mono-, di- and tri-substituted  $\alpha$ -  
peptides,  $\beta$ -peptides,  $\gamma$ -peptides,  $\omega$ -peptides, peptides wherein  
the amino acid residues are in the L-form or in the D-form,  
vinyllogous polypeptides, glycopoly-peptides, polyamides,  
vinyllogous sulfonamide peptides, polysulfonamides, conjugated  
peptides ~~comprising e.g. prosthetic groups~~, polyesters,  
polysaccharides, polycarbamates, polycarbonates, polyureas,  
polypeptidylphosphonates, polyurethanes, azatides, oligo N-  
substituted glycines, polyethers, ethoxyformacetal oligomers,  
poly-thioethers, polyethylene glycols (PEG), polyethylenes,  
polydisulfides, polyarylene sulfides, polynucleotides, PNAs,  
LNAs, morpholinos, oligo pyrrolinones, polyoximes, polyimines,  
polyethyleneimines, polyimides, polyacetals, polyacetates,  
polystyrenes, polyvinyl, lipids, phospholipids, glycolipids,  
polycyclic compounds ~~comprising e.g. aliphatic or aromatic  
cycles, including polyheterocyclic compounds, proteoglycans,  
and polysiloxanes~~, and combinations thereof,

wherein each molecule is synthesised by reacting a  
plurality of chemical entities in the range of from 2 to 200.



13-45 (Cancelled).

46. (Previously Presented) The method of claim 1, wherein the reaction of chemical entities involve at least two reactive groups of at least one chemical entity.

47. (Previously Presented) The method of claim 1, wherein each connector oligonucleotide comprises or consists of a sequence of nucleotides.

48. (Previously Presented) The method of claim 1, each connector oligonucleotide having from 3 to 30 nucleotides.

49-51 (Cancelled).

52. (Previously Presented) The method of claim 1, wherein at least one of said building blocks comprise a chemical entity comprising a scaffold moiety comprising a plurality of reactive groups.

53. (Original) The method of claim 52, wherein said scaffold moiety reactive groups react with one or more chemical entities of a single building block, or with one or more chemical entities of different building blocks.

54-80 (Cancelled).

81. (Previously Presented) The method of claim 1, wherein at least one chemical entity reaction is an acylation reaction.

82. (Currently Amended) The method of claim 1, wherein at least one chemical entity comprises an amine, and wherein an amide bond is formed when at least one chemical ~~entity~~ entity is reacted.

83-84 (Cancelled).

85. (Currently Amended) A method for generating a library of bifunctional complexes comprising a molecule and an identifier polynucleotide capable of identifying the chemical entities having participated in the synthesis of the molecule,

or identifying the reaction steps having led to the synthesis of the molecule, said method comprising the steps of

hybridising a plurality of building block identifier oligonucleotides to a plurality of connector oligonucleotides each capable of hybridising to one or more building block oligonucleotides, said building block identifier oligonucleotides being linked to one or more chemical entities,

covalently linking said building block oligonucleotides hybridised to one or more connector oligonucleotides, thereby generating a plurality of identifier polynucleotides linked to a plurality of non-reacted chemical entities,

separating the identifier polynucleotides from the optionally ligated connector oligonucleotides, preferably by degrading the optionally ligated connector oligonucleotides and/or by performing a washing step wherein the identifier polynucleotides are associated with a solid support capable of being separated from non-bound, optionally ligated connector oligonucleotides[[]]

reacting chemical entities linked to each of a plurality of different identifier polynucleotides, and

generating a library of bifunctional complexes each comprising a different molecule and an identifier polynucleotide identifying the chemical entities having participated in the synthesis of the molecule,

wherein each of the plurality of molecules are generated by reacting at least 2 chemical entities associated with different building block oligonucleotides.

86-173 (Cancelled).

174. (Currently Amended) A method for synthesising a plurality of different molecules, said method comprising  
(1) providing a plurality of connector oligonucleotides each capable of hybridizing to at least 1 complementary connector oligonucleotide,

(2) providing a plurality of complementary connector oligonucleotides selected from the group consisting of

- a) complementary connector oligonucleotides comprising at least 1 chemical entity comprising at least 1 reactive group,
- b) complementary connector oligonucleotides comprising at least 1 reactive group,
- c) complementary connector oligonucleotides comprising at least 1 spacer region,

(3) hybridizing the plurality of connector oligonucleotides and complementary connector oligonucleotides, thereby forming a plurality of different hybridisation complexes, each hybridisation complex comprising at least 2 complementary connector oligonucleotides and at least 2 connector oligonucleotides,

wherein, for each of said hybridisation complexes,

at least 2 of said complementary connector oligonucleotides comprise at least 1 chemical entity comprising at least 1 reactive group, and

at least 1 of said complementary connector oligonucleotides hybridizes to at least 2 connector oligonucleotides, and

(4) ligating, enzymatically, chemically, or otherwise, complementary connector oligonucleotides, thereby forming identifier polynucleotides, wherein each identifier polynucleotide is associated with a plurality of unreacted chemical entities,

(5) separating each identifier polynucleotide associated with unreacted chemical entities from optionally ligated connector oligonucleotides associated therewith, and

(6) reacting, when the identifier polynucleotides are no longer hybridised to the optionally ligated connector oligonucleotides, at least 2 chemical entity reactive groups of each identifier polynucleotide ~~identifier~~ by reacting at least 1 reactive group of each chemical entity,

wherein, for each bifunctional complex, the reaction of said chemical entity reactive groups results in the formation of a different molecule by reacting at least 2 chemical entities provided by separate complementary connector oligonucleotides, thereby synthesising a plurality of different molecules.

175. (Original) The method of claim 174 comprising the further step of selecting molecules having desirable

characteristics, wherein the selection employs a predetermined assaying procedure.

176. (Previously Presented) The method of claim 174 comprising the further step of amplifying at least part of the individual and optionally ligated connector oligonucleotides used for the formation of the initial hybridisation complexes.

177. (Original) The method of claim 176 comprising the further step of contacting a population of said amplified, optionally ligated connector oligonucleotides, or fragments thereof, with a plurality of building block oligonucleotides.

178. (Currently Amended) The method of claim 177 comprising the further step of performing an additional synthesis round by carrying out the steps ~~of the method of the invention~~ (1)-(6) using, as the provided connector oligonucleotides of step (1), a population of said amplified connector oligonucleotides, or a population of said amplified connector oligonucleotide fragments.